

WHAT IS CLAIMED IS:

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- ~~1. A pharmaceutical composition, comprising formoterol, or a derivative thereof, in a pharmacologically suitable fluid, wherein the composition is stable during long term storage and the fluid comprises water.~~
 2. The pharmaceutical composition of claim 1, wherein the composition has an estimated shelf-life of greater than 1 month usage time at 25 °C and greater than or equal to 1 year storage time at 5 °C.
 3. The pharmaceutical composition of claim 2, wherein greater than about 80% of the initial formoterol is present after 1 month usage time at 25 °C and 1 year storage time at 5 °C.
 4. The pharmaceutical composition of claim 1 that has been nebulized.
 5. The pharmaceutical composition of claim 1, wherein the pharmacologically suitable fluid comprises a polar solvent.
 6. The pharmaceutical composition of claim 5, wherein the polar solvent is a protic solvent.
 7. The pharmaceutical composition of claim 6, further comprising a tonicity adjusting agent.
 8. The pharmaceutical composition of claim 7, wherein the tonicity adjusting agent is ammonium carbonate, ammonium chloride, ammonium lactate, ammonium nitrate, ammonium phosphate, ammonium sulfate, ascorbic acid, bismuth sodium tartrate, boric acid, calcium chloride, calcium disodium edetate, calcium gluconate, calcium lactate, citric acid, dextrose, diethanolamine, dimethylsulfoxide, edetate disodium, edetate trisodium monohydrate, fluorescein sodium, fructose, galactose, glycerin, lactic acid, lactose, magnesium chloride, magnesium sulfate, mannitol, polyethylene glycol, potassium acetate, potassium chlorate, potassium chloride, potassium iodide, potassium nitrate, potassium phosphate, potassium sulfate, propylene glycol, silver nitrate, sodium acetate, sodium bicarbonate, sodium biphosphate, sodium bisulfite,
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- sodium borate, sodium bromide, sodium cacodylate, sodium carbonate, sodium chloride, sodium citrate, sodium iodide, sodium lactate, sodium metabisulfite, sodium nitrate, sodium nitrite, sodium phosphate, sodium propionate, sodium succinate, sodium sulfate, sodium sulfite, sodium 5 tartrate, sodium thiosulfate, sorbitol, sucrose, tartaric acid, triethanolamine, urea, urethan, uridine or zinc sulfate.

9. The pharmaceutical composition of claim 8, wherein the tonicity adjusting agent is sodium chloride.

10. The pharmaceutical composition of claim 1, wherein the 10 pharmacologically suitable fluid comprises a buffer.

11. The pharmaceutical composition of claim 10, wherein the buffer is citric acid/phosphate, acetate, barbital, borate, Britton-Robinson, cacodylate, citrate, collidine, formate, maleate, McIlvaine, phosphate, Prideaux-Ward, succinate, citrate-phosphate-borate (Teorell-Stanhagen), 15 veronal acetate, MES (2-(N-morpholino)ethanesulfonic acid), BIS-TRIS (bis(2-hydroxyethyl)iminotris(hydroxymethyl)methane), ADA (N-(2-acetamido)-2-iminodiacetic acid), ACES (N-(carbamoylmethyl)-2-aminoethanesulfonic acid), PIPES (piperazine-N,N'-bis(2-ethanesulfonic acid)), MOPSO (3-(N-morpholino)-2-hydroxypropanesulfonic acid), BIS- 20 TRIS PROPANE (1,3-bis(tris(hydroxymethyl)methylamino)propane), BES (N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid), MOPS (3-(N-morpholino)propanesulfonic acid), TES (N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid), HEPES (N-(2-hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid), DIPSO (3-(N,N-bis(2-hydroxyethyl)amino)-2- 25 hydroxypropanesulfonic acid), MOBS (4-(N-morpholino)butanesulfonic acid), TAPSO (3-(N-tris(hydroxymethyl)methylamino)-2-hydroxypropanesulfonic acid), tris(hydroxymethylaminomethane, HEPPSO (N-(2-hydroxyethyl)piperazine-N'-(2-hydroxypropanesulfonic acid), POPSO (piperazine-N,N'-bis(2-hydroxypropanesulfonic acid)), TEA 30 (triethanolamine), EPPS (N-(2-hydroxyethyl)piperazine-N'-(3-propane-sulfonic acid), TRICINE (N-tris(hydroxymethyl)methylglycine), GLY-GLY

(glycylglycine), BICINE (N,N-bis(2-hydroxyethyl)glycine), HEPBS (N-(2-hydroxyethyl)piperazine-N'-(4-butanesulfonic acid)), TAPS (N-tris(hydroxymethyl)methyl-3-aminopropanesulfonic acid), or AMPD (2-amino-2-methyl-1,3-propanediol) buffer.

- 5 12. The pharmaceutical composition of claim 11, wherein the buffer is citrate buffer.
13. The pharmaceutical composition of claim 12, wherein the buffer concentration is from about 0.01 mM to about 150 mM.
14. The pharmaceutical composition of claim 13, wherein the
10 buffer concentration is from about 1 mM to about 20 mM.
15. The pharmaceutical composition of claim 14, wherein the buffer concentration is about 5 mM.
16. The pharmaceutical composition of claim 8, wherein the ionic strength of the composition is about 0 to about 0.4.
- 15 17. The pharmaceutical composition of claim 16, wherein the ionic strength of the composition is about 0.05 to about 0.16.
18. The pharmaceutical composition of claim 1, wherein the pH of the composition is about 2.0 to about 8.0.
19. The pharmaceutical composition of claim 18, wherein the pH
20 of the composition is about 4.0 to about 6.0.
20. The pharmaceutical composition of claim 19, wherein the pH of the composition is about 4.5 to about 5.5.
21. The pharmaceutical composition of claim 20, wherein the pH of the composition is about 5.0.
- 25 22. The pharmaceutical composition of claim 1, wherein the formoterol free base concentration is about 5 μ g/mL to about 2 mg/mL.
23. The pharmaceutical composition of claim 22, wherein the formoterol free base concentration is about 10 μ g/mL to about 1 mg/mL.
24. The pharmaceutical composition of claim 23, wherein the
30 formoterol free base concentration is about 50 μ g/mL to about 200 μ g/mL.

25. The pharmaceutical composition of claim 24, wherein the formoterol free base concentration is about 59 $\mu\text{g}/\text{mL}$.

26. The pharmaceutical composition of claim 24, wherein the formoterol free base concentration is about 118 $\mu\text{g}/\text{mL}$.

5 27. The pharmaceutical composition of claim 8, further comprising a buffer.

28. The pharmaceutical composition of claim 27, wherein the buffer is citric acid/phosphate, acetate, barbital, borate, Britton-Robinson, cacodylate, citrate, collidine, formate, maleate, McIlvaine, phosphate,
10 Prideaux-Ward, succinate, citrate-phosphate-borate (Teorell-Stanhagen), veronal acetate, MES (2-(N-morpholino)ethanesulfonic acid), BIS-TRIS (bis(2-hydroxyethyl)iminotris(hydroxymethyl)methane), ADA (N-(2-acetamido)-2-iminodiacetic acid), ACES (N-(carbamoylmethyl)-2-aminoethanesulfonic acid), PIPES (piperazine-N,N'-bis(2-ethanesulfonic
15 acid)), MOPSO (3-(N-morpholino)-2-hydroxypropanesulfonic acid), BIS-TRIS PROPANE (1,3-bis(tris(hydroxymethyl)methylamino)propane), BES (N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid), MOPS (3-(N-morpholino)propanesulfonic acid), TES (N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid), HEPES (N-(2-hydroxyethyl)piperazine-N'-(2-
20 ethanesulfonic acid), DIPSO (3-(N,N-bis(2-hydroxyethyl)amino)-2-hydroxypropanesulfonic acid), MOBS (4-(N-morpholino)butanesulfonic acid), TAPSO (3-(N-tris(hydroxymethyl)methylamino)-2-hydroxypropanesulfonic acid), tris(hydroxymethylaminomethane), HEPPSO (N-(2-hydroxyethyl)piperazine-N'-(2-hydroxypropanesulfonic acid)), POPSO
25 (piperazine-N,N'-bis(2-hydroxypropanesulfonic acid)), TEA (triethanolamine), EPPS (N-(2-hydroxyethyl)piperazine-N'-(3-propanesulfonic acid), TRICINE (N-tris(hydroxymethyl)methylglycine), GLY-GLY (glycylglycine), BICINE (N,N-bis(2-hydroxyethyl)glycine), HEPBS (N-(2-hydroxyethyl)piperazine-N'-(4-butanesulfonic acid)), TAPS (N-tris(hydroxy-
30 methyl)methyl-3-aminopropanesulfonic acid), or AMPD (2-amino-2-methyl-1,3-propanediol) buffer.

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29. The pharmaceutical composition of claim 28, wherein the buffer is citrate buffer.
30. The pharmaceutical composition of claim 29, wherein the buffer concentration is from about 0.01 mM to about 150 mM.
- 5 31. The pharmaceutical composition of claim 30, wherein the buffer concentration is from about 1 mM to about 20 mM.
32. The pharmaceutical composition of claim 31, wherein the buffer concentration is about 5 mM.
33. The pharmaceutical composition of claim 27, wherein the
10 ionic strength of the composition is about 0 to about 0.4.
34. The pharmaceutical composition of claim 33, wherein the ionic strength of the composition is about 0.05 to about 0.16.
35. The pharmaceutical composition of claim 27, wherein the pH of the composition is about 2.0 to about 8.0.
- 15 36. The pharmaceutical composition of claim 35, wherein the pH of the composition is about 4.0 to about 6.0.
37. The pharmaceutical composition of claim 36, wherein the pH of the composition is about 4.5 to about 5.5.
38. The pharmaceutical composition of claim 37, wherein the pH
20 of the composition is about 5.0.
39. The pharmaceutical composition of claim 27, wherein the formoterol free base concentration is about 5 µg/mL to about 2 mg/mL.
40. The pharmaceutical composition of claim 39, wherein the formoterol free base concentration is about 10 µg/mL to about 1 mg/mL.
- 25 41. The pharmaceutical composition of claim 40, wherein the formoterol free base concentration is about 50 µg/mL to about 200 µg/mL.
42. The pharmaceutical composition of claim 41, wherein the formoterol free base concentration is about 59 µg/mL.
- 30 43. The pharmaceutical composition of claim 41, wherein the formoterol free base concentration is about 118 µg/mL.

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44. The pharmaceutical composition of claim 25 that has been nebulized.
45. The pharmaceutical composition of claim 26 that has been nebulized.
- 5 46. The pharmaceutical composition of claim 42 that has been nebulized.
47. The pharmaceutical composition of claim 43 that has been nebulized.
- 10 48. The pharmaceutical composition of claim 27 that has been nebulized.
49. The pharmaceutical composition of claim 42, wherein the buffer is citrate buffer.
50. The pharmaceutical composition of claim 42, wherein the buffer concentration is about 5 mM.
- 15 51. The pharmaceutical composition of claim 42, wherein the ionic strength of the composition is about 0.05 to about 0.16.
52. The pharmaceutical composition of claim 42, wherein the pH of the composition is about 5.0.
- 20 53. The pharmaceutical composition of claim 42, wherein the buffer is citrate buffer; the buffer concentration is about 5 mM; the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.
54. The pharmaceutical composition of claim 43, wherein the buffer is citrate buffer.
- 25 55. The pharmaceutical composition of claim 43, wherein the buffer concentration is about 5 mM.
56. The pharmaceutical composition of claim 43, wherein the ionic strength of the composition is about 0.05 to about 0.16.
- 30 57. The pharmaceutical composition of claim 43, wherein the pH of the composition is about 5.0.

58. The pharmaceutical composition of claim 43, wherein the buffer is citrate buffer; the buffer concentration is about 5 mM; the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

5 59. The pharmaceutical composition of claim 53 that has been nebulized.

60. The pharmaceutical composition of claim 58 that has been nebulized.

10 61. A nebulized solution, comprising formoterol or a derivative thereof in a pharmacologically suitable fluid.

62. A kit, comprising:

(a) an aqueous composition comprising formoterol or a derivative thereof formulated for single dosage administration; and

15 (b) a nebulizer.

63. The kit of claim 62, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 59 μ g/mL; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 5 mM;

20 wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

64. The kit of claim 62, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 118 μ g/mL; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 5 mM;

25 wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

65. A combination, comprising:

30 (a) the pharmaceutical composition of claim 1 formulated for single dosage administration; and—
(b) a vial.

66.3 The combination of claim 65, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 59 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 5 mM;

5 wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

67.4 The combination of claim 65, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 118 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c)

10 citrate buffer at a concentration of about 5 mM;

wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

68. A method for the treatment, prevention, or amelioration of one or more symptoms of bronchoconstrictive disorders, comprising

15 administering an effective amount of the pharmaceutical composition of claim 1 to a subject in need of such treatment.

69. A method for the treatment, prevention, or amelioration of one or more symptoms of bronchoconstrictive disorders, comprising administering an effective amount of the pharmaceutical composition of

20 claim 53 to a subject in need of such treatment.

70. A method for the treatment, prevention, or amelioration of one or more symptoms of bronchoconstrictive disorders, comprising administering an effective amount of the pharmaceutical composition of claim 58 to a subject in need of such treatment.

71. An article of manufacture, comprising packaging material, an aqueous composition comprising the composition of claim 1 formulated for single dosage administration, which is useful for treatment, prevention or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction, and a

30 label that indicates that the composition is used for treatment, prevention

or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction.

- ~~72.6~~ An article of manufacture, comprising packaging material, the composition of claim 53 formulated for single dosage administration,
- 5 which is useful for treatment, prevention or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction, and a label that indicates that the composition is used for treatment, prevention or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or
- 10 uncontrolled bronchoconstriction.

- ~~73.6~~ An article of manufacture, comprising packaging material, the composition of claim 58 formulated for single dosage administration, which is useful for treatment, prevention or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or
- 15 uncontrolled bronchoconstriction, and a label that indicates that the composition is used for treatment, prevention or amelioration of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction.

74. ~~The method of claim 68, further comprising administering~~
- 20 one or more of (a) to (j) as follows: (a) a β_2 -adrenoreceptor agonist; (b) a dopamine (D₂) receptor agonist; (c) an IL-5 inhibitor; (d) an antisense modulator of IL-5; (e) a tryptase inhibitor; (f) a tachykinin receptor antagonist; (g) milrinone or milrinone lactate; (h) a leukotriene receptor antagonist; (i) a 5-lipoxygenase inhibitor; or (j) an anti-IgE antibody;
- 25 simultaneously with, prior to or subsequent to the formoterol composition.

75. ~~The method of claim 69, further comprising administering~~
- one or more of (a) to (j) as follows: (a) a β_2 -adrenoreceptor agonist; (b) a dopamine (D₂) receptor agonist; (c) an IL-5 inhibitor; (d) an antisense
- 30 modulator of IL-5; (e) a tryptase inhibitor; (f) a tachykinin receptor antagonist; (g) milrinone or milrinone lactate; (h) a leukotriene receptor

antagonist; (i) a 5-lipoxygenase inhibitor; or (j) an anti-IgE antibody; simultaneously with, prior to or subsequent to the formoterol composition.

76. The method of claim 70, further comprising administering
5 one or more of (a) to (l) as follows: (a) a β_2 -adrenoreceptor agonist; (b) a dopamine (D₂) receptor agonist; (c) an IL-5 inhibitor; (d) an antisense modulator of IL-5; (e) a tryptase inhibitor; (f) a tachykinin receptor antagonist; (g) milrinone or milrinone lactate; (h) a leukotriene receptor antagonist; (i) a 5-lipoxygenase inhibitor; or (j) an anti-IgE antibody;
10 simultaneously with, prior to or subsequent to the formoterol composition.

77. The pharmaceutical composition of claim 1, further comprising one or more of (a) to (j) as follows: (a) a β_2 -adrenoreceptor agonist; (b) a dopamine (D₂) receptor agonist; (c) an IL-5 inhibitor; (d) an
15 antisense modulator of IL-5; (e) a tryptase inhibitor; (f) a tachykinin receptor antagonist; (g) milrinone or milrinone lactate; (h) a leukotriene receptor antagonist; (i) a 5-lipoxygenase inhibitor; or (j) an anti-IgE antibody.

78. The pharmaceutical composition of claim 11, wherein the
20 buffer comprises citric acid/phosphate buffer, acetate buffer, citrate buffer or phosphate buffer.

79. The pharmaceutical composition of claim 27, wherein the buffer comprises citric acid/phosphate buffer, acetate buffer, citrate buffer or phosphate buffer.

80. The pharmaceutical composition of claim 13, wherein the
25 buffer concentration is from about 1 mM to about 50 mM.

81. The pharmaceutical composition of claim 80, wherein the buffer concentration is about 20 mM.

82. The pharmaceutical composition of claim 30, wherein the
30 buffer concentration is from about 1 mM to about 50 mM.

14 83. The pharmaceutical composition of claim 82, wherein the buffer concentration is about 20 mM.

15 84. The pharmaceutical composition of claim 42, wherein the buffer concentration is about 20 mM.

5 85. The pharmaceutical composition of claim 42, wherein the buffer is citrate buffer; the buffer concentration is about 20 mM; the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

10 86. The pharmaceutical composition of claim 43, wherein the buffer concentration is about 20 mM.

16 87. The pharmaceutical composition of claim 43, wherein the buffer is citrate buffer; the buffer concentration is about 20 mM; the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

15 88. The pharmaceutical composition of claim 85 that has been nebulized.

17 89. The pharmaceutical composition of claim 87 that has been nebulized.

20 90. The kit of claim 62, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 59 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 20 mM;

wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

25 91. The kit of claim 62, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 118 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 20 mM;

wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

81 92. The combination of claim 65, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 59 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c) citrate buffer at a concentration of about 20 mM;

5 wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

82 93. The combination of claim 65, wherein the aqueous composition comprises (a) formoterol free base at a concentration of about 118 $\mu\text{g}/\text{mL}$; (b) aqueous saline comprising sodium chloride; and (c)

10 citrate buffer at a concentration of about 20 mM;

wherein the ionic strength of the composition is about 0.05 to about 0.16; and the pH of the composition is about 5.0.

83 94. The pharmaceutical composition of claim 1, further comprising an anticholinergic agent.

15 84 95. The pharmaceutical composition of claim 94, wherein the anticholinergic agent is ipratropium bromide, oxitropium bromide, atropine methyl nitrate, tiotropium bromide or glycopyrronium bromide.

85 96. The pharmaceutical composition of claim 95, wherein the anticholinergic agent is ipratropium bromide.

20 86 97. The pharmaceutical composition of claim 96, wherein the ipratropium bromide is present at a concentration of about 5 $\mu\text{g}/\text{mL}$ to about 5 mg/mL.

87 98. The pharmaceutical composition of claim 95, wherein the anticholinergic agent is tiotropium bromide.

25 88 97. The pharmaceutical composition of claim 96, wherein the tiotropium bromide is present at a concentration of about 5 $\mu\text{g}/\text{mL}$ to about 5 mg/mL.